

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

JUAN JOSE LEGARDA IBANEZ

Serial No. 10/622,068

Filed: July 15, 2003

For: Use of Flumazenil in the
Production of a Medicament for
the Treatment of Cocaine Dependency)



Art Unit: 1614

Examiner: Not yet assigned

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PETITION TO ACCELERATE EXAMINATION UNDER MPEP 708.02 VIII

Mail Stop Petition
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Applicant hereby petitions under MPEP 708.02 VIII to accelerate examination of the above-identified application. Pursuant to this section, Applicant provides the following information.

1) A listing of claims directed to a single invention appears on **Page 2** of this Petition.

2) A statement that a pre-examination search was made, appears on **Page 4** of this Petition. A copy of the search is attached as Exhibit A.

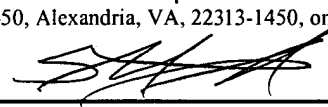
3) A discussion of the references which points out how the subject matter is patentable over the references begins on **Page 5** of this Petition.

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I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, VA, 22313-1450, on March 1, 2006.


Stephen C. MacDonald, Ph.D. - Reg. No. L0063

Claims Listing

Claims 1-18. (Cancelled)

19. (Previously presented) A method for treating cocaine dependency, comprising administering a therapeutically effective amount of flumazenil to a patient in need of such treatment.
20. (Previously presented) The method of claim 19, wherein the flumazenil is administered sequentially at short time intervals in small quantities.
23. (Previously presented) The method of claim 19, wherein the flumazenil is administered at time intervals of between about one and about fifteen minutes.
24. (Previously presented) The method of claim 19, wherein the flumazenil is administered in quantities between about 0.1 and about 0.3 mg.
25. (Previously presented) The method of claim 19, wherein the flumazenil is administered at time intervals of between about one and about fifteen minutes in quantities between about 0.1 and about 0.3 mg.
26. (Previously presented) The method of claim 19, wherein the effective amount of flumazenil is between about 1.5 and about 2.5 mg/day.
27. (Previously presented) The method of claim 19, wherein about 0.2 mg of flumazenil is administered sequentially at intervals of about 3 minutes.
28. (Previously presented) The method of claim 19, wherein the flumazenil is administered orally or parenterally.
29. (Previously presented) The method of claim 28, wherein the parenteral administration of flumazenil is intravenous administration.
30. (Previously presented) The method of claim 19, wherein the flumazenil is administered before, during or after treatment with an additional agent.
31. (Previously presented) The method of claim 30, wherein the additional agent is clomethiazole.
32. (Previously presented) The method of claim 30, wherein the additional agent is selected from the group consisting of Vitamin B Complex, Piracetam, vitamins, minerals, proteins, amino acids, disulfiram, fluoxetine, and combinations thereof.

33. (Previously presented) The method of claim 19, wherein the flumazenil is administered under sedation.
34. (Previously presented) The method of claim 19, wherein the administration of flumazenil reduces or eliminates the desire to use cocaine.
35. (Previously presented) A method for treating cocaine dependency, comprising administering a therapeutically effective amount of flumazenil to a patient in need of such treatment, wherein the flumazenil is administered at time intervals of between about one and about fifteen minutes in quantities between about 0.1 and about 0.3 mg.
36. (Previously presented) The method of claim 35, wherein the effective amount of flumazenil is between about 1.5 and about 2.5 mg/day.
37. (Previously presented) The method of claim 35, wherein the administration of flumazenil reduces or eliminates the desire to use cocaine.

Search Results

Applicant states herein that a pre-examination search was conducted during the international stage of this application PCT/ES02/00061. MPEP 708.02 (VIII) permits the entry of the International Search Report to satisfy this requirement. A copy of the International Search Report is attached as Exhibit A. The articles cited in the International Search Report were disclosed in the Information Disclosure Statement filed May 13, 2005. A supplemental Information Disclosure Statement was filed on September 7, 2005 disclosing further references potentially relevant to this application. Copies of the references were made of record when filing the Information Disclosure Statements.

Discussion of References Cited

International Search Report References

The claims are directed to a method of treating cocaine dependency comprising administering flumazenil. None of the references disclose the use of flumazenil to treat cocaine *dependency*. These references disclose the use of flumazenil to treat acute cocaine *toxicity or poisoning*.

Supplemental IDS references

There were 43 references cited in the supplemental IDS pertaining generally to the use of flumazenil in conditions other than cocaine dependency, for example GABA receptor structure and pharmacology.

References 10, 13, 14, 19, 25, 28-30, and 32-35 are not prior art since they were published after the priority date, but illustrate the state of the art.

References 1, 23, 24, 26, 27, 31, and 42 provide a characterization of GABA receptors and the properties of the subunits that form the GABA receptors. None of these references disclose the treatment of cocaine dependency using flumazenil.

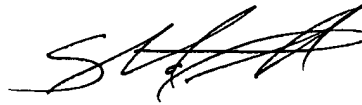
References 2, 4-9, 11, 12, 15, 16, 18, 20, 22, 36-38, 41 and 43 provide a characterization of GABA receptor pharmacology. None of these references disclose the treatment of cocaine dependency using flumazenil.

References 3, 17, 21, 39 and 40 describe the actions of flumazenil on reducing GABA receptor subunit expression, pain, hyperphagia or anxiety, but do not disclose the treatment of cocaine dependency.

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Applicant respectfully requests accelerated prosecution of this application having satisfied the requirements of MPEP 708.02 (VIII). Form PTO-2038 is enclosed herewith authorizing the charge of \$130.00 for the fee required under 37 C.F.R. §1.17 (h). The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Deposit Account No. 11-0855.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'S. MacDonald', is written over the typed name.

Stephen C. MacDonald, Ph.D.
Patent Agent
Reg. No. L0063

Kilpatrick Stockton LLP
1100 Peachtree Street
Suite 2800
Atlanta, Georgia 30309-4530
Our Docket: 55979-0200(314570)

INFORME DE BÚSQUEDA INTERNACIONAL

Solicitud internacional n°
PCT/ ES 02/00061

| A. CLASIFICACIÓN DEL OBJETO DE LA SOLICITUD CIP ⁷ A61P 25/30, A61K 31/5517 De acuerdo con la Clasificación Internacional de Patentes (CIP) o según la clasificación nacional y la CIP. | | |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|
| B. SECTORES COMPRENDIDOS POR LA BÚSQUEDA Documentación mínima consultada (sistema de clasificación, seguido de los símbolos de clasificación) CIP ⁷ Otra documentación consultada, además de la documentación mínima, en la medida en que tales documentos formen parte de los sectores comprendidos por la búsqueda Bases de datos electrónicas consultadas durante la búsqueda internacional (nombre de la base de datos y, si es posible, términos de búsqueda utilizados) EPDOC, WPI, REGISTRY, CA, MEDLINE, BIOSIS | | |
| C. DOCUMENTOS CONSIDERADOS RELEVANTES | | |
| Categoría* | Documentos citados, con indicación, si procede, de las partes relevantes | Relevante para las reivindicaciones n° |
| X | UKI, F. y col. The effect of Flumazenil administration on acute cocaine intoxication of rats. Arukoru Kenkyu to Yakubutsu Izon, 1994, Vol. 29, N° 2, páginas 92-102. ISSN 0389-4118. (resumen) HCAPLUS (en línea) (recuperado el 2002-03-18). Recuperado de: STN International, Columbus, Ohio (EE.UU). N° de acceso de Hcaplus 1994:595617. | 1-18 |
| X | DERLET, R.W. y col. Anticonvulsivant modification of cocaine-induced toxicity in the rat. Neuropharmacology. 1990, Vol 29, N° 3, páginas 255-259, ISSN 0028-3908. Resumen; página 256, columna 2, líneas 3-; página 257, tabla 1. | 1-18 |
| <input checked="" type="checkbox"/> En la continuación del recuadro C se relacionan otros documentos <input type="checkbox"/> Los documentos de familia de patentes se indican en el anexo | | |
| * Categorías especiales de documentos citados: "A" documento que define el estado general de la técnica no considerado como particularmente relevante. "B" solicitud de patente o patente anterior pero publicada en la fecha de presentación internacional o en fecha posterior. "L" documento que puede plantear dudas sobre una reivindicación de prioridad o que se cita para determinar la fecha de publicación de otra cita o por una razón especial (como la indicada). "O" documento que se refiere a una divulgación oral, a una utilización, a una exposición o a cualquier otro medio. "P" documento publicado antes de la fecha de presentación internacional pero con posterioridad a la fecha de prioridad reivindicada. "T" documento ulterior publicado con posterioridad a la fecha de presentación internacional o de prioridad que no pertenece al estado de la técnica pertinente pero que se cita por permitir la comprensión del principio o teoría que constituye la base de la invención. "X" documento particularmente relevante; la invención reivindicada no puede considerarse nueva o que implique una actividad inventiva por referencia al documento aisladamente considerado. "Y" documento particularmente relevante; la invención reivindicada no puede considerarse que implique una actividad inventiva cuando el documento se asocia a otro u otros documentos de la misma naturaleza, cuya combinación resulta evidente para un experto en la materia. "&" documento que forma parte de la misma familia de patentes. | | |
| Fecha en que se ha concluido efectivamente la búsqueda internacional. 26 Abril 2002 | | Fecha de expedición del informe de búsqueda internacional 21 MAY 2002 21. 05. 02 |
| Nombre y dirección postal de la Administración encargada de la búsqueda internacional O.E.P.M. C/ Panamá 1, 28071 Madrid, España. N° de fax +34 91 3495304 | | Funcionario autorizado E. Albarrán n° de teléfono + 34 91 349 5595 |

INFORME DE BÚSQUEDA INTERNACIONAL

PCT/ ES 02/00061

| C (Continuación). DOCUMENTOS CONSIDERADOS RELEVANTES | | |
|------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|
| Categoría * | Documentos citados, con indicación, si procede, de las partes relevantes | Relevante para las reivindicaciones n° |
| A | DERLET, R. W. y col. Flumazenil induces seizures and death in mixed Cocaine-Diazepam intoxications. Annals of emergency medicine. 1994, Vol. 23, N° 3, páginas 494-498, ISSN 0196-0644. Resumen. | 1-18 |
| A | MALBRAIN, M.L. y col. A massive, near-fatal Cocaine intoxication in a body-stuffer. Acta Clinica Belgium. 1994, Vol. 49, N° 1, páginas 12-18, ISSN 0001-5512. Resumen; página 16, párrafo 2. | 1-18 |
| A | WOOLF, A. Cocaine poisoning. Clinical toxicology review.. Mayo 1995, Vol. 18, N° 8. Capítulo "Tratamiento" párrafo 5. | 1-18 |

INFORME DE BÚSQUEDA INTERNACIONAL

Solicitud internacional n°

PCT/ES 02/00061

Recuadro I Observaciones cuando se estime que algunas reivindicaciones no pueden ser objeto de búsqueda (Continuación del punto 2 de la primera hoja)

De conformidad con el artículo 17.2.a), algunas reivindicaciones no han podido ser objeto de búsqueda por los siguientes motivos:

1. ☒ Las reivindicaciones n°s: 10-18 se refieren a un objeto con respecto al cual esta Administración no está obligada a proceder a la búsqueda, a saber: las reivindicaciones 10-18 se refieren a un método de tratamiento terapéutico aplicado al cuerpo humano; a pesar de ello la búsqueda se ha realizado para dichas reivindicaciones en base a los efectos atribuidos al compuesto.
2. ☐ Las reivindicaciones n°s: se refieren a elementos de la solicitud internacional que no cumplen con los requisitos establecidos, de tal modo que no pueda efectuarse una búsqueda provechosa, concretamente:
3. ☐ Las reivindicaciones n°s: son reivindicaciones dependientes y no están redactadas de conformidad con los párrafos segundo y tercero de la regla 6.4.a).

Recuadro II Observaciones cuando falta unidad de invención (Continuación del punto 3 de la primera hoja)

La Administración encargada de la Búsqueda Internacional ha detectado varias invenciones en la presente solicitud internacional, a saber:

1. ☐ Dado que todas las tasas adicionales han sido satisfechas por el solicitante dentro del plazo, el presente informe de búsqueda internacional comprende todas las reivindicaciones que pueden ser objeto de búsqueda.
2. ☐ Dado que todas las reivindicaciones que pueden ser objeto de búsqueda pueden serlo sin un esfuerzo particular que justifique una tasa adicional, esta Administración no ha invitado al pago de ninguna tasa de esta naturaleza.
3. ☐ Dado que tan sólo una parte de las tasas adicionales solicitadas ha sido satisfecha dentro del plazo por el solicitante, el presente informe de búsqueda internacional comprende solamente aquellas reivindicaciones respecto de las cuales han sido satisfechas las tasas, concretamente las reivindicaciones n°s:
4. ☐ Ninguna de las tasas adicionales solicitadas ha sido satisfecha por el solicitante dentro de plazo. En consecuencia, el presente informe de búsqueda internacional se limita a la invención mencionada en primer término en las reivindicaciones, cubierta por las reivindicaciones n°s:

Indicación en cuanto a la reserva ☐ Las tasas adicionales han sido acompañadas de una reserva por parte del solicitante.
☐ El pago de las tasas adicionales no ha sido acompañado de ninguna reserva.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/ ES 02/00061

| C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|-------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| A | DERLET, R. W. y col. Flumazenil induces seizures and death in mixed Cocaine-Diazepam intoxications. Annals of emergency medicine. 1994, Vol. 23, N° 3, pages 494-498, ISSN 0196-0644. Abstract. | 1-18 |
| A | MALBRAIN, M.L. y col. A massive, near-fatal Cocaine intoxication in a body-stuffer. Acta Clinica Belgica. 1994, Vol. 49, N° 1, pages 12-18, ISSN 0001-5512. Abstract ; page 16, paragraph 2. | 1-18 |
| A | WOOLF, A. Cocaine poisoning. Clinical toxicology review. May 1995, Vol. 18, N° 8. Chapter "Tratamiento" paragraph 5. | 1-18 |

INTERNATIONAL SEARCH REPORT

International application No.
PCT/ ES 02/00061

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 10-18
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 10-18 relate to a therapeutic treatment method that is carried out on the human body. Nevertheless, the search on said claims was carried out and was based on the effects attributed to the compound.
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/ ES 02/00061

| A. CLASSIFICATION OF SUBJECT MATTER | | |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|
| IPC ⁷ A61P 25/30, A61K 31/5517 | | |
| According to International Patent Classification (IPC) or to both national classification and IPC | | |
| B. FIELDS SEARCHED | | |
| Minimum documentation searched (classification system followed by classification symbols) | | |
| IPC ⁷ | | |
| Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched | | |
| Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) | | |
| EPODOC, WPI, REGISTRY, CA, MEDLINE, BIOSIS | | |
| C. DOCUMENTS CONSIDERED TO BE RELEVANT | | |
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X | UKI, F. y col. The effect of Flumazenil administration on acute cocaine intoxication of rats. Arukoru Kenkyu to Yakubutsu Izon, 1994, Vol. 29, N° 2, pages 92-102. ISSN 0389-4118. (abstract) HCAPLUS (line) (recovered the 2002-03-18). recovered from: STN International, Columbus, Ohio (U.S.A). access N° of Hcaplus 1994:595617. | 1-18 |
| X | DERLET, R.W. y col. Anticonvulsivant modification of cocaine-induced toxicity in the rat. Neuropharmacology. 1990, Vol 29, N° 3, pages 255-259, ISSN 0028-3908. abstract ; page 256, column 2, lines 3-; page 257, table 1. | 1-18 |
| <input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex. | | |
| <p>* Special categories of cited documents:</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"I" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</p> <p>"&" document member of the same patent family</p> | | |
| Date of the actual completion of the international search | | Date of mailing of the international search report |
| 26 April 2002 (26.04.02) | | 21 May 2002 (21.05.02) |
| Name and mailing address of the ISA/ | | Authorized officer |
| S.P.T.O | | |
| Facsimile No. | | Telephone No. |

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